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Docket No.: H1890.0200

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Gary D. Hodgen et al.

Application No.: 09/313,625

Filed: May 18, 1999

Art Unit: 1617

For: CONTROL OF SELECTIVE ESTROGEN RECEPTOR MODULATORS

Examiner: E. J. Webman

APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the Notice of Non-Compliant Appeal Brief mailed January 10, 2006, submitted herewith is the Appeal Brief originally filed on December 13, 2004 which has been revised as noted in the next paragraph.

The Notice indicates that the concise explanation of the subject matter defined in the independent claims makes reference to the relevant page number of the specification but does not identify line numbers – line numbers have been added. The Notice states the brief does not present an argument under a separate heading for each ground of rejection – while there is only one such ground and there was a heading ("argument"), an additional heading has been added. Finally, the Notice says the Appendix A containing the appealed claims is not of record – the image file wrapper of

this case shows Appendix A is in fact of record and correctly sets forth the claims on appeal but to avoid any potential argument, a section setting forth the withdrawn claims, not on appeal, has been added.

This brief contains items under the following headings as required by 37 C.F.R. § 41.37 and M.P.E.P. § 1206:

I. REAL PARTY IN INTEREST

The real party in interest for this appeal is the Eastern Virginia Medical School

II. RELATED APPEALS, INTERFERENCES, AND JUDICIAL PROCEEDINGS

There are no other appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

There are 13 claims pending in application. Claims 3-9 and 11 have been withdrawn from consideration but have not canceled. Claims 1, 2, 10, 12, and 13 have been rejected and are the subject of this appeal.

IV. STATUS OF AMENDMENTS

Applicant did not amend the claims after the final rejection.

V. SUMMARY OF CLAIMED SUBJECT MATTER

As pointed out on page 4, lines 8-14, of the application, the use of a selective estrogen receptor modulator (SERM) in hormone replacement therapy (HRT) was known prior to the present invention. As is also known, HRT is administered to women who have gone through or are going through menopause, an event which causes infertility as a result of normal aging, i.e., the women are or are about to be infertile (Id.). The SERMs have their own side effects, one of which is bleeding (page 1, lines 25-29; page 3, lines 14-21). The presently claimed invention is based on improving the known HRT method using a SERM by additionally administering an agent which exhibits progestogenic activity to the woman receiving HRT in an amount effective to modulate the side effects of the SERM (page 48-20).

VI. GROUNDS OF OBJECTION TO BE REVIEWED ON APPEAL

Claims 1, 2, 10, 12 and 13 have been rejected under 35 U.S.C. § 103(a) over Young (US 4,729,999) in view of Peters (US 5,116,895).

VII. ARGUMENT

The Invention Recited in Claims 1, 2, 10, 12 and 13 is Unobvious

Hormone replacement therapy (HRT) involves administration of hormones to women who have gone through or are going through menopause, an event which causes infertility as a result of normal aging, i.e., the women are or are about to be infertile. The use of a selective estrogen receptor modulator (SERM) in HRT has been known from a time prior to the present invention, as pointed out on page 4 of the application. That prior art is acknowledged by the preamble of the Jepson claims of this case. However, it is also known, as also explained on pages 1-3 of the application, that the SERMs have their own side effects, such as stimulation of endometrial development, one manifestation of which is bleeding. The presently claimed invention improves the known HRT method using a SERM by additionally administering an agent which exhibits progestogenic activity to the woman receiving HRT in an amount effective to modulate the side effects of the SERM. The progestin modulates the stimulation of the endometrium caused by the SERM, which in turn, modulates the bleeding manifestation of SERM administration.

The use of a progestin to modulate the stimulation of the endometrium caused by the SERM and thereby the bleeding manifestation of SERM administration is not made obvious by the references applied in the rejection under consideration in this appeal.

The primary reference, Young, teaches the use of a SERM in HRT. As such, Young simply teaches nothing more than the method which is being improved in the present invention, i.e., the method set forth in the preamble of the instant claims. There is no teaching or suggestion of combating the side effects of the SERM in this reference.

Since there is no teaching or suggestion concerning any side effects of the SERM, the reference cannot provide any motivation to address them.

The Peters reference was first cited in the Final Rejection. It relates to certain novel progestins. The entire relevant disclosure in Peters is found in the first column where it is indicated that known progestins, as well as the new compounds,

> . . . find a wide range of beneficial applications in human therapy. Such applications include, for example, in addition to suppressing ovulation, control of uterine bleeding, treatment of amenorrhea and dysmenorrheal, alleviation of endocrine disorders, and treatment of infertility. (column 1, lines 36-41)

The rejection under consideration is predicated on the assertion that Peters teaches that progestins such as levonorgestrel have been used for to control uterine bleeding (final rejection, page 2). However, what is meant by the expression "control of uterine bleeding" is never stated in this reference.

While the meaning of "control" is not discussed in Peters, it is apparent from the fact that the passage making reference to "control" is sandwiched between a paragraph referring to menstruation and a paragraph referring to contraception, that what is being controlled is the normal uterine bleeding of a pre-menopausal woman. There is no reference in Peters to HRT (normally administered to post-menopausal women) and clearly, therefore, addressing bleeding which is a side-effect of a SERM administered in the course of HRT was clearly never contemplated. Nothing in Peters suggests administering anything, much less a progestin, to control SERM induced bleeding. Nothing in Peters suggests to one skilled in the art that any progestin may have some effect on such bleeding.

Uterine bleeding is normally understood in the art to refer to cycle (menstrual) control and/or dysfunction and breakthrough bleeding and spotting. All of

these are normal or not unusual events for pre-menopausal women. The claimed invention is not concerned with such uterine bleeding.

At the very best, it could be argued that the broad and undefined reference to "control of uterine bleeding" in Peters might, perhaps, make it obvious to try to employ a progestin in connection with a SERM HRT procedure in order to determine if such usage would address the bleeding side effect of the SERM. "Obvious to try" is, however, is insufficient under § 103. Moreover, It is respectfully submitted that it requires reliance on speculation to even assert that the Peters disclosure rises to the level of obvious to try. The reference teaches in column 2 that progestins per se can have an estrogenic or an anti-estrogenic effect. When added to a SERM, as proposed in the rejection, will they impart an estrogenic effect, and thereby make estrogenic bleeding worse, or an anti-estrogenic effect? There is no basis for conjecture of record.

In the Advisory Action, the Examiner observed that Peters refers to other activity of progestins but that observation is not relevant to the appealed claims.

The combination of references advanced in the rejection under consideration does not render the claimed invention obvious. Accordingly, the rejection under 35 U.S.C. § 103 should be reversed.

VIII. CLAIMS

A copy of the claims involved in the present appeal is attached hereto as Appendix A.

IX. STATEMENT ABOUT EVIDENCE APPENDIX

No Evidence Appendix is present because no evidence pursuant to §§ 1.130, 1.131, or 1.132 or entered by or relied upon by the examiner was submitted.

IX. STATEMENT ABOUT RELATED APPEALS AND INTERFERENCES APPENDIX

No related proceedings are referenced in II. above, and hence no Appendix thereof is included.

Respectfully submitted,

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APPENDIX A

Claims Involved in the Appeal of Application Serial No. 09/313,625

1. In a method of hormone replacement therapy comprising administering an effective amount of a selective estrogen receptor modulator to a woman in need of such therapy in order to control and regulate estrogenic impact on specific tissues and organs, the improvement which comprises additionally administering an agent which exhibits progestogenic activity in the woman in an amount which is effective to modulate the bleeding side effects of the selective estrogen receptor modulator.

2. The method of claim 1 wherein the selective estrogen receptor modulator is clomiphene.

10. The method of claim 1 wherein the agent which exhibits progestogenic expresses both androgenic and progestogenic activity.

12. The method of claim 10 wherein the agent which exhibits progestogenic is a single material which expresses both activities.

13. The method of claim 12 wherein the agent which exhibits progestogenic is danazol or levonorgestrel.

Claims Withdrawn and Therefore Not On Appeal

2. The method of claim 1 wherein the selective estrogen receptor modulator is clomiphene.

3. The method of claim 1 wherein the selective estrogen receptor modulator is a benzothiophene.

4. The method of claim 1 wherein the agent which exhibits progestogenic is an antiprogestin.

5. The method of claim 4 wherein the antiprogestin is a progesterone receptor antagonist.

6. The method of claim 5 wherein the selective estrogen receptor modulator is clomiphene.

7. The method of claim 5 wherein the selective estrogen receptor modulator is a benzothiophene.

8. The method of claim 4 wherein the amount of antiprogestin is that sufficient to maintain the blood estrogen concentration in the range of about 25 to 125 pg/ml.

9. The method of claim 8 wherein the amount of antiprogestin is that sufficient to maintain the blood estrogen concentration in the range of about 60 to 90 pg/ml.

11. The method of claim 10 wherein the agent which exhibits progestogenic comprises the combination of an androgen and a progestin.